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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,231	08/19/2004	Paul Richard Gellert	ASZD-P01-724	3886

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,231	GELLERT ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendments and arguments, filed 11/1/2006, have been fully considered entered into the record. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. However, upon further consideration the following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. In light of the new rejections being applied against the pending claims, this Office Action is Non-Final.

Status of the Claims

Claims 1-19 are currently pending and are the subject of this Office Action. All claims are presently amended.

Information Disclosure Statement

Examiner has received and considered the information disclosure statements (IDS) submitted under 37 C.F.R. § 1.97(b) on 8/4/2006 and 37 C.F.R. § 1.97(c) on 11/1/2006. Please see attached USPTO Form 1449.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. In the instant case, the claims recite the limitation "will substantially completely dissolve" (*e.g.* claim 1, line 6). This limitation is indefinite because the metes and bounds of the claim limitation are not clear and concise as required by 35 U.S.C. § 112, 2nd Paragraph. It is not clear what applicant intends the phrase "substantially completely" to encompass. "Completely" means 100%. The modifier "substantially" has not been defined in the claim or specification. As such, it is not apparent to what degree "substantially" modifies the limitation "completely".

Claims 1-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case, claim 1 recites parenthetical information (*e.g.* "the Agent"). The information in parentheses is deemed indefinite because it can be interpreted as a claim limitation.

Claim 19 is rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: steps wherein the claimed method reduces inter-patient variability. Claim 19 only recites that the composition of claim 1, 7 or 12 is administered to a patient. However, the claim is drawn to a method for reducing inter-patient variability. It is not clear how simply administering a composition to a patient will reduce inter-patient variability.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gibson (U.S. Patent No. 5,770,599; Issued Jun. 23, 1998) in view of Thosar *et al.* (U.S. Patent No. 6,410,054; Issued Jun. 25, 2002; Filed Dec. 8, 1999).[1]

The instant claims recite pharmaceutical compositions comprising 4-(3'-chloro-4'-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline (*i.e.* Iressa® or gefitinib) and a water-soluble cellulose ether or ester of a water-soluble cellulose ether. Examiner has interpreted the limitations added in the amendment to claim 1 to mean that the composition is intended for immediate release (*i.e.* not sustained or extended release). This interpretation is supported by applicant's arguments, filed 11/1/2006 wherein they state, "Applicant's claimed composition is not a sustained release formulation and the claims have been amended to more clearly indicate this fact..." (pages 11-12).

Gibson discloses the instantly claimed compound (col. 8, lines 61-64). It is further disclosed that the compounds exemplified in the reference can be formulated into pharmaceutical

[1] As discussed in the Office Action mailed 8/1/2006, the instant claims are afforded a priority date of June 11, 2002 (filing date of foreign priority document 0213267.8). As such, Gibson qualifies as prior art under 35 U.S.C. § 102(b) and Thosar *et al.* qualify as prior art under 35 U.S.C. § 102(e)(2).

compositions in association with a pharmaceutically acceptable diluent or carrier (col. 13, line 65 to col. 14, line 3; Claim 17). The composition may be in a form suitable for oral administration, for example as a tablet or capsule (col. 13, lines 4-5). The compositions may be prepared in conventional manners using conventional excipients (*id.* at lines 10-11). The instant claims differ from the Gibson disclosure in that they recite specific excipients and proportions of excipients to active agent.

Thosar *et al.* disclose immediate release formulations of eplerenone so as to provide a readily soluble form of eplerenone (Abstract; col. 2, lines 39-40). The compositions disclosed therein provide "unique combinations" of carrier materials that provide better solubilization characteristics, improved bioavailability, chemical stability, dissolution profiles, disintegration times and improved pharmacokinetics (*id.* at lines 51-58; col. 3, line 46 to col. 4, line 14). The compositions can be formulated in a form suitable for oral administration comprising 1% to 95% active agent (col. 6, lines 40-41 and 44-49). Such oral forms can further comprise buffering agents and can be prepared with enteric coatings (*id.* at lines 62-65). Carriers include agents that improve dissolution and disintegration profiles, hardness, crushing strength and friability (col. 8, lines 29-36). Diluents are present in amounts ranging from 5% to 99% and can include lactose, mannitol and microcrystalline cellulose (*id.* at lines 38-59). Disintegrants are present in amounts ranging from 0.5% to 30% and include celluloses, such as methylcellulose, sodium carboxymethylcellulose and carboxymethylcellulose (col. 9, lines 9-27). Binding agents include povidone, present in an amount of 0.5% to 25% (*id.* at lines 33-55). Hydroxypropyl methylcellulose is a preferred binding agent, present in a range of 0.5% to 10% (*id.* at lines 56-62). Additional excipients are disclosed at col. 10, line 6 to col. 11, line 41. The immediate

release compositions preferably release 90% of the active agent within 45 minutes using 0.1 N HCl in water at 37 °C (col. 13, line 65 to col. 14, line 16). Suitable coating materials include hydroxypropyl methylcellulose as instantly claimed (col. 20, lines 19-27). An immediate release composition comprising active agent and hydroxypropyl methylcellulose is shown in Example 3 (col. 36, lines 25-50). The reference thus teaches immediate release pharmaceutical compositions comprising the instantly claimed excipients.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

In the instant case, Gibson teaches that the instantly claimed compound can be formulated into pharmaceutical compositions comprising conventional excipients. Thosar *et al.* teach that the instantly claimed excipients were known in the art to be useful in immediate release compositions. As such, one skilled in the art motivated to formulate an immediate release composition of 4-(3'-chloro-4'-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline would reasonably expect that the excipients present in the compositions taught in Thosar *et al.* could be predictably used with any active agent, including those taught in Gibson.

As such, absent a demonstration of unexpected results commensurate in scope with the claims, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to formulate a composition of 4-(3'-chloro-4'-fluoroanilino)-7-methoxy-6-

(3-morpholinopropoxy)quinazoline and water-soluble cellulose ethers. The skilled artisan would have been highly motivated to formulate a composition wherein the composition improves bioavailability, stability, dissolution profiles, disintegration times, etc. as taught in Thosar *et al.*

With regard to claims that recite specific concentration and ratios of the components, it is the position of the examiner that such limitations do not impart patentability absent a showing of criticality. The prior art discloses compositions comprising the active agent and excipients of the recited claims. Applicant is reminded that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. See *In re Aller*, 220 F.2d 454 105 USPQ 233,235 (CCPA 1955).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson, Ph.D.
Patent Examiner
AU 1614

February 16, 2007

PHYLLIS SPIVACK
PRIMARY EXAMINER